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10/566,903	10/16/2006	Gurjit K. Khurana Hershey	CMC-170	1134

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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,903	HERSHEY ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *17-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 7 in the reply filed on 5/12/09 is acknowledged. Upon further consideration, the restriction among groups 1-7 is WITHDRAWN. The election of species set forth in the paragraph numbered four in the restriction requirement mailed 10/566,903 is WITHDRAWN. Applicant traverses the restriction on the grounds that there is not an undue burden to examine all of the claims. This is not found persuasive because this application is filed under 35 USC 371, and unity of invention standard applies, and thus a showing of lack of unity is required for proper restriction of claims and such a showing has been made. Applicant has not argued that the showing of lack of unity of invention was improper. The requirement is maintained and made FINAL.

2. Claims 1-16 and 25-27 as presented in the Article 34 amendment received on 6/6/05 with the letter of 2/6/05 are examined herein (see notation in IPER).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 2-4, 5, 6, and 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 requires "determining at least one of IL-4Rα, IL-13, or a CD14 promoter from at least one cell" but it is unclear what it means to "determine" IL-4Rα or any of the other recited molecules. Further, this method step is inclusive of determining only one of

those three listed subjects, yet the "wherein" clause that follows the recitation of the step refers to combinations of what appear to be alleles from two or three different molecules as indicating an increased propensity to a food allergen. It is not known what it means for "an excess" of particular combinations to be present in a single individual. This is not an art appreciated term, and its meaning is not clearly defined in the specification. The claim recites that an excess of VV-QR AND QR-TT indicate an individual's increase propensity to food allergy- but it is not clear if applicant intends to require that both of these genotypes are detected, or if applicant intends to state that either one of them indicates propensity for food allergy. The use of the conjunction "and" suggests that both must be present, however, the format of the claim suggests that only one must be present. Either way, it is reiterated that the current claims require determining only one of IL-4Rα, IL-13, or a CD14 promoter.

In claim 2 it is not clear what it means for there to be an increase of the allele combination over a control because a single individual would be expected to have only two copies of each gene, so the use of the phrase "an increase relative to a control" is misplaced in this context. It appears from the teachings of the specification that the presence of the IL4-Rα 75V, IL-13 130Q, and CD14 -159T genotype is indicative of increased propensity to food allergy relative to individuals that do not have this combination of alleles, so applicant is advised to consider amending the claims to reflect this finding more precisely. For example, see enabled scope lettered (D) in the scope of enablement rejection in this office action.

Claim 5 is confusing because it states that an increased propensity to a food allergy is present if the TT genotype differs from a control, because either a particular

genotype is related to a disease or indicative of a phenotype is not a matter of comparing a single individual's genotype to a control, but instead it is a matter of an underlying relationship existing to support the finding of increased propensity. Applicant is advised to consider amending the claim to reflect suggested language in (A) in the listing of enabled scope provided in this office action. Claims 6, 7, 8, 9, and 10 are likewise confusing because they also refer to comparing the markers present in a single individual to a control as a basis for determining increased propensity to food allergy.

Claim 16 is indefinite because it is not clear what it means for a variant to be "in" a particular allele, and as a result it is not clear what applicant is intending the claim to require.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Assa'ad et al. (2001, as cited in IDS).

The single method step in this claim requires determining at least one of IL-4Rα, IL-13, or a CD14 promoter from at least one cell in an individual. Assa'ad et al. teach genotyping IL-13, and teach that the Q130 allele occurs with higher frequency in patients

with food allergy than in non-atopic subjects, and that the allele may confer susceptibility to food allergy.

7. Claims 1, 5, 7, 8, and 10 rejected under 35 U.S.C. 102(a) as being anticipated by Woo et al. (J Allergy Clin Immunol, Vol. 111, No. 4, page 907).

Woo et al. teach genotyping the -159 C to T polymorphism in CD14, and they both teach that the TT genotype of the polymorphism is associated with food allergy.

This rejection applies to claim 1 because the single method step in claim 1 requires determining at least one of IL-4Rα, IL-13, or a CD14 promoter from at least one cell in an individual, and Woo et al. clearly anticipate that step.

This rejection applies to claim 10 because the further limitation does not appear to be an active process step, and thus does not modify the single method step of the claim which is "determining in at least one cell of the individual a single nucleotide polymorphism marker (SNP) in -159 C→T CD14."

8. Claims 11, 12, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Howell et al. (Clinical and Experimental Allergy, 1998, Volume 28, pages 156-162).

Howell et al. teach analyzing at least one cell of an individual in at least a two-locus analysis, and to be specific, in a three locus analysis. Namely, Howell et al. teach analyzing the HLA class II loci DRB1, DQB1, and DPB1 (pages 157-158, and throughout), and the identification of alleles in each of these genes that are associated with peanut allergy. Regarding claim 13, these alleles are broadly considered "atopy-associated" because they were shown to be associated with "peanut allergy" phenotype that includes atopic peanut allergy.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 6 and 11, 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Assa'ad et al. in view of either Woo et al. (J Allergy Clin Immunol, Vol. 111, No. 4, page 907).

Assa'ad et al. teach genotyping IL-13, and teach that the Q130 allele occurs with higher frequency in patients with food allergy than in non-atopic subjects, and that the allele may confer susceptibility to food allergy.

Assa'ad et al. do not teach analysis of a second marker.

Woo et al. teach genotyping the -159 C to T polymorphism in CD14, and they both teach that the TT genotype of the polymorphism is associated with food allergy.

It would have been prima facie obvious to one of ordinary skill in the art to have determined the genotype of a single individual at both marker positions in order to provide a more complete means for profiling the individual for markers for food allergy.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1, 11, 12, 13, and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims all recite methods where molecules are analyzed for the presence of alleles that are indicative of food allergy in individuals. The specification discloses detecting the presence of particular genotypes that were demonstrated to be present in a population of individuals that have food allergies more commonly than in a population of individuals who do not have allergies (i.e. detecting the TT genotype in the individual at position -159 of the CD14 gene; detecting the presence of genotype VVQR in the individual at wherein the VV is present at position 75 of IL-4Rα and QR is present at position 130 of IL-13; detecting the presence of genotype QRTT in the individual at wherein the QR is present at position 130 of IL-13 and TT is present at position -159 of the CD14 gene; and detecting the presence of genotype V-Q-T in the individual at wherein the V is present at position 75 of IL-4Rα, the Q is present at position 130 of IL-13, and T is present at position -159 of the CD14 gene). However, the claims at issue encompass the detection of additional polymorphic positions within IL-4Rα, IL-13, or a CD14 or within undisclosed genes.

The specification does not disclose any structure or physical and/or chemical characteristic that would readily allow one skilled in the art to identify additional naturally occurring polymorphisms that are related to an increased likelihood of the presence of food allergies. All members of the genus of markers to be detected have the same function, i.e. they are associated with increased propensity for the presence of food allergy, but no correlation between naturally occurring structures and their common

feature is disclosed. The question is whether one of skill in the art would be able to distinguish members of the subgenus of polymorphic markers associated with food allergy from other members of the genus of polymorphic markers.

The nature of alleles is that they are variant structures, and in the present state of the art, the structure of one allele does not provide guidance to the existence or structure of other alleles. In other words, the existence and structure of other alleles are not predictable from the one species of allele described. The description given is not adequate to allow one of skill in the art to distinguish members of the claimed subgenus from other members of the genus. One of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the species in the genus and is insufficient to support the claim.

13. Claims 1, 6, 7, 9, 10, 11, 12, 13, 14, 15, and 25-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

> (A) A method for determining an individual has an increased propensity for food allergy, said method comprising detecting the presence of a TT genotype in the individual at position -159 of the CD14 gene, and determining that the individual has an increased propensity for food allergy if this genotype is present, wherein the increase is relative to individuals that do not have the TT genotype.
>
> (B) A method for determining an individual has an increased propensity for food allergy, said method comprising detecting the presence of genotype VVQR in the individual at wherein the VV is present at position 75 of IL-4Rα and QR is present at position 130 of IL-13, and determining that the individual has an increased propensity for food allergy if this genotype is present, wherein the increase is relative to individuals that do not have the genotype.
>
> (C) A method for determining an individual has an increased propensity for food allergy, said method comprising detecting the presence of genotype QRTT in the individual at wherein the QR is present at position 130 of IL-13 and TT is present at position -159 of the CD14 gene, and determining that the individual has an increased propensity for food allergy if this genotype is present, wherein the increase is relative to individuals that do not have the genotype.

(D) A method for determining an individual has an increased propensity for food allergy, said method comprising detecting the presence of genotype V-Q-T in the individual at wherein the V is present at position 75 of IL-4Rα, the Q is present at position 130 of IL-13, and T is present at position -159 of the CD14 gene, and determining that the individual has an increased propensity for food allergy if this genotype is present, wherein the increase is relative to individuals that do not have the genotype.

does not reasonably provide enablement for methods which rely on the detection of other genotypes, or methods which positively detect that allergy is present. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches that the TT genotype at position -159 of CD14 was associated with food allergy, but that no significant allele frequency difference between food allergy patients and normal controls was found (p. 5, lines 3-4). The specification teaches that the V-Q-T allele combination occurred more frequently in patients with allergy than without, and that this result was significant (p. 13). However, the specification teaches that the number of individuals carrying the V-R-T allele combination was not significantly different between patients and controls (p. 13). This exemplifies that it is highly unpredictable which genotypes or individual alleles of IL-4Rα, IL-13, or a CD14 are associated with increased propensity for the presence of food allergy. By extension, it is also highly unpredictable which alleles of other genes or of unidentified polymorphisms within these genes are indicative of increased propensity for the presence of food allergy.

Claim 1 is unclear, as is previously discussed in this office action. Nonetheless, as it is currently written, it requires only the determination of one of the particular molecules recited, and further the active process step is silent as to what about those molecules is determined, i.e. the claim is silent as to what position or polymorphic section of the molecule is being analyzed, and so is sufficiently broad in the active process step so as to encompass determining any aspect of the recited molecules. However, it is highly unpredictable which positions within these genes are polymorphic, and even once additional polymorphic positions are determined, which alleles would be indicative of increased propensity for food allergy. The instant specification supports that this technology area is highly unpredictable when it teaches "a given SNP may only be relevant in the context of a second or a combination of additional SNP in the same gene or other genes...a given SNP may have no effect individually or in combination with a different set of SNPs. Genetic association studies may be difficult to interpret due to poor reproducibility in other populations. One reason for this may be that a given genetic variant may not be important unless it is examined in the context of one or more additional SNPs (p. 16, lines 21 and following)."

The language of claim 6 is inclusive of determining food allergy by detecting a SNP in any pair wise combination of two genes, determining polymorphisms from each of those genes, with the genes and polymorphisms specified in the claims. However, it is highly unpredictable based on the teachings of the specification which pair wise combinations of alleles would be indicative increased propensity to allergy. The specification teaches that the allele combinations recited in (C) and (D) above are predictably related to increased propensity to allergy, but the specification is silent, for

example as to any predictive relationship between alleles at positions 400, 431, or 576 of IL-4Rα and their predictive relationship with food allergy. It is entirely unpredictable based on the teachings in the specification (or the lack thereof) as to whether these polymorphisms can be used in combination with R130Q of IL-13 or C→T of CD14 to predict increased propensity for food allergy.

Claims 7, 9, and 10 are inclusive of making a prediction based on the presence of any possible allele combination at the C→T CD14 polymorphic position, as the claims are silent as to what allele or genotype is detected in order to indicate an increased propensity to a food allergy. The specification teaches, however, that only the TT allele was found to be differently present in individuals with allergy relative to healthy controls. The difference at the genotype level was not statistically significant- i.e. the presence of only one "T" was not sufficient to differentiate between tests and controls.

Claims 11 and 13 are sufficiently broad so as to encompass the analysis of any two loci, and likewise claim 12 is sufficiently broad so as to encompass the analysis of any three loci. The context of the claims clearly requires that these loci are related to an individual's propensity to have food allergy. The specification provides evidence regarding only those relationships set forth as (A) through (D) in this relationship. It is highly unpredictable as to what additional two or three loci combinations may exist in the entirety of the human genome that would function in the claimed methods. Claim 14 requires that at least two of the IL-4Rα, IL-13, or a CD14 genes is analyzed, but is silent as to which portion of the gene is analyzed. As discussed in relation to claim 1, it is highly unpredictable which positions within these genes are polymorphic, and even once additional polymorphic positions are determined, which alleles would be indicative of

increased propensity for food allergy. Claim 15 requires that two variants from a list of those given are analyzed. The problematic nature of this breadth has been discussed with regard to claim 6.

Claims 25, 26, and 27 are all drawn to methods for positively identifying individuals with peanut, milk, or food allergies, solely on the basis of the presence of the combination of particular markers present in the individual. However, for each of the recited allele combinations, the specification teaches that while allele frequencies differed between patients with and without allergies, the allele combinations were present in individuals without allergy. This then, demonstrates that a method which identifies the presence of allergies solely on the basis of the presence of the combination of markers listed in these claims would not be functional, as it is not reflective of the data presented in the specification. Thus, although claims similar to these, where increased propensity for food allergy are enabled as set forth in (A)-(D) above, these claims which are drawn to a method for identifying an individual with a particular allergy are not enabled.

It would take an enormous amount of experimentation in order to provide sufficient guidance to practice the claims commensurate in scope with their current breadth. One would have to undertake many studies of polymorphisms in the IL-4Rα, IL-13, or a CD14 genes to identify additional polymorphisms that are associated with food allergy, if they exist. For claims 11-13 this experimentation would not be limited to any particular gene, but would amount to trial and error experimentation and testing of the entire genome. All of this experimentation would take place in the context of a technology area that is entirely unpredictable as associations between polymorphisms and genes can only be determined empirically. Thus, it is concluded that it would require

undue experimentation to practice the claimed invention commensurate in scope with these claims.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Tuesday or Wednesday, from 9:00 AM until 4:30 PM, and Thursday afternoon from 12:30 PM until 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached by calling (571) 272-0763.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

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/Juliet C. Switzer/
Primary Examiner
Art Unit 1634

June 19, 2009